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KATE H. MURASHIGE
MORRISON & FOERSTER LLP
3811 VALLEY CENTRE DRIVE
SUITE 500
SAN DIEGO CA 92130-2071

EXAMINER	
BASI,N	
ART UNIT	PAPER NUMBER
1646	26

DATE MAILED: 10/23/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/030482	Terrance P. Snutch
Examiner	**Group Art Unit**
Nirmal SBasi	1646

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Response

A SHORTENED STATUTORY PERIOD FOR RESPONSE IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a response be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for response specified above is less than thirty (30) days, a response within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for response is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to respond within the set or extended period for response will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☐ Responsive to communication(s) filed on 9/5/01.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 28-34 is/are pending in the application.

Of the above claim(s) 34 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 28-33 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 16

☐ Interview Summary, PTO-413

☐ Notice of References Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other _____

Office Action Summary

DETAILED ACTION

1. The request filed on 9/5/01 for a Continued Prosecution Application (CPA) under 37 CFR 1.53 (d) based on parent application No. 09/030,482 is accepted and a CPA has been established. An action on the CPA follows

2. Amendment filed 4/9/01, Amendment filed 6/11/01 and Declaration filed 6/11/01 have been entered.

Response to Amendment with new claims

3. Applicant has canceled claims 16-27, previously present in the Application and amended claims 28-33 and added new claim 34. Newly added claims 34, will not be examined. Since applicant has received an action on the merits for the originally presented invention (Group I), this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 34, drawn to a method to obtain an isolated DNA molecule encoding a functional α1 subunit of a T-type calcium channel, using PCR is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejection, 35 U.S.C. 112, second paragraph

4. Claims 28-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 28 is indefinite because "Medium hybridization stringency" conditions are not disclosed. The metes and bounds of the group of sequences that would meet the limitations of the

claim depend upon the precise conditions under which hybridizations were performed including wash conditions. Applicants arguments and the disclosure by Dr. Terry P. Snutch does not overcome the examiners rejection because the hybridization and wash conditions dictate which DNA sequences remain specifically bound to the nucleic acid encoding the polypeptide of SEQ ID NO:18, the metes and bounds of the claims cannot be determined without the disclosure of said conditions. The disclosure by Dr. Terry P. Snutch does not overcome the deficiency in the specification which does not disclose "Medium hybridization stringency", used in instant claims. The specification nor claims disclose the "medium hybridization stringency" conditions. For example, what is the salt concentration, temperature , time etc. encompassed by the claim.

Claim 28, 32 and 33 are indefinite because it is not clear what is the "functional T-type" calcium channel α1 subunit, so as to allow the metes and bounds of the claims to be determined. The specification and Applicants Response filed 6/11/01 disclose the "amino acid sequence encoded by SEQ ID NO:18 is not complete", and lacks a small portion of the amino acid sequence which is required to obtain functionality (See paper number 23, page 4, second paragraph). What else in addition to the monomer is required form the "functional tetrameric form". The name α_1 subunit does not sufficiently serve to characterize said polypeptide. The application has disclosed a partial sequences for the polynucleotide encoding the polypeptide of SEQ ID NOs:19. The name $\alpha\text{-}_1$ subunit encompasses the complete sequence of the protein and therefore does not sufficiently serve to characterize said protein. Without knowledge of the structure and function of the claimed subunit the metes and bounds of the claim cannot be determined.

Claims 28 is indefinite because SEQ ID NO:18 is nucleic acid not polypeptide, as inferred by the claim.

Claims 29 is indefinite because SEQ ID NO:18 is nucleic acid, not polypeptide as inferred by the claim.

Claims 30-31 are indefinite for depending on a base claim or intermediate claim and fail to resolve the issues raised above.

In instances where reference has been made to SEQ ID NO:18 as polypeptide, Examiner will refer to said SEQ ID NO: as SEQ ID NO:19. SEQ ID NO:18 is polynucleotide and SEQ ID NO:19 is the polypeptide.

5. ***Response to 35 USC § 101 and 35 USC § 112, 1st paragraph Claim Rejections***

Applicant and the Declaration of Dr. Snutch (6/11/01) have argued that a specific or substantial utility has been provided in the specification and the Examiner reconsider and withdraw the rejection. Applicants and the Declaration of Dr. Snutch have been fully considered but not found persuasive. The specification discloses the polypeptide is incomplete and lacking functionality. Applicants Response filed 6/11/01 verifies the "amino acid sequence encoded by SEQ ID NO:18 is **not complete**", and **lacks a portion of the amino acid sequence which is required to obtain functionality** (See paper number 23, page 4, second paragraph). Therefore, by Applicants own admission, the claimed polynucleotide encoding the polypeptide of SEQ ID NO:18, is incomplete. Applicant further admits, page 6, the **polypeptide is missing "approximately 400 amino acids"**. Even though the missing sequence may turn out to be homologous or similar to the C-terminus of

other cannel proteins, further experimentation is required to complete the missing sequence. Further, once the missing sequence is determined, further experimentation is required to determine functionality. The possibility exists that other sub-units may have to be discovered which are required to confer functionality on the α1 subunit. Applicant has generally argued that claimed invention can be used to screen for compounds which agonize or antagonize the T-type calcium ion channel and that antagonists of this channel are useful in treating specific conditions. Applicant has not disclosed any antagonists that are useful or any specific conditions treatable with said antagonists. Without knowledge of the functionality of the claimed invention, it is not clear to the Examiner, how one can make the assumption that an antagonist will treat a specific condition. Applicant has generally argued the general nature of calcium channels and in essence verifies the Examiners position to the complex nature of calcium signaling, the diversity of the effects of calcium in signaling mechanisms and the effects of the various calcium channels in signaling mechanisms is dependent on the specific calcium channel.

Applicant further argues the use of claimed invention as biological target for screening libraries of compounds as candidate pharmaceuticals. Applicant claims the claimed invention has a clear nexus to specific disease states and "All of the T-type calcium ion channels have the same connection to disease states". Applicants arguments have been fully considered but not found persuasive. As disclosed above the calcium channels have diverse effects. Applicant has not disclosed any specific disease state involve in dysfunction of claimed invention.

Applicants arguments have been fully considered but not found persuasive.

The instant application does not disclose the biological role of the polypeptide of SEQ ID NO:19 or its significance. Applicant asserts that the invention has numerous practical, beneficial uses in toxicology testing, drug development, and diagnosis of disease, none of which necessarily require detailed knowledge of how the polypeptide coded for by the polynucleotide works.

These utilities are not considered to be specific and substantial because the specification fails to disclose any particular function or biological significance for the claimed polynucleotide. The disclosed protein, whose cDNA has been isolated, is said to have a potential function based upon its amino acid sequence similarity to other known proteins. After further research, a specific and substantial credible utility might be found for the claimed polynucleotide. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete.

The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility. The court held that:

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion.

The instant claims are drawn to a protein of as yet undetermined function or biological significance. There is no evidence of record or any line of reasoning that would support a conclusion that the claimed polynucleotide was, as of the filing date, useful for diagnosis, prevention and treatment of an disease, or for screening compounds. Until some actual and specific significance can be attributed to the protein identified in the specification as SEQ ID NO:19, or the gene encoding it, one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Thus, there was no immediately apparent or "real world" utility as of the filing date.

The DNA of the instant invention and the protein encoded thereby are compounds which share some structural similarity to receptor proteins having calcium channel proteins based on sequence similarity. As disclosed by the specification and Applicants response the family of calcium proteins may have diverse effects, and play roles in the pathogenesis of various diseases, require other subunits for binding of ligands Although the family of receptor proteins having calcium protein like domains may share some common structural motifs, various members of the family may have different sites of action and different biological effects. In the absence of knowledge of the ligand for claimed invention, or the biological significance of this protein, there is no immediately evident

patentable use. To employ a protein of the instant invention in any of the disclosed methods would clearly be using it as the object of further research. Such a use has been determined by the courts to be a utility which, alone, does not support patentability. Since the instant specification does not disclose a credible "real world" use for claimed polynucleotide, then the claimed invention as disclosed does not meet the requirements of 35 U.S.C. §101 as being useful.

Further Applicant has argued that the claims provide a meaningful structural limitation and functional language. The specification not claims disclose what is the critical structure of the invention that is required for functionality. Since applicant has admitted that the claimed polynucleotide is incomplete and does not contain a complete polypeptide, lacks functionality, therefore, the functional limitation has not been met. As regards the structural limitation, the hybridization conditions specified do not provide a meaningful structural limitation, see rejection under 35 USC 112, second paragraph, above.

For a utility to be "well-established" it must be specific, substantial and credible. All nucleic acids and genes are in some combination useful in toxicology testing. However, the particulars of toxicology testing with SEQ ID NO:18 or 19 are not disclosed in the instant specification. Neither the toxic substances nor the susceptible organ systems are identified. Therefore, this is a utility which would apply to virtually every member of a general class of materials, such as any collection of proteins or DNA, but is only potential with respect to SEQ ID NO:18 and SEQ ID NO:19. Because of this, such a utility is not specific and does not constitute a "well-established" utility. Further, because any potential diagnostic utility is not yet known and has not yet been disclosed, the utility is

not substantial because it is not currently available in practical form. Moreover, use of the claimed polynucleotide in an array for toxicology screening is only useful in the sense that the information that is gained from the array is dependent on the pattern derived from the array, and says nothing with regard to each individual member of the array. Again, this is a utility which would apply to virtually ever member of a general class of materials, such as any collection of proteins or DNA. Even if the expression of Applicants' individual polynucleotide is affected by a test compound in an array for drug screening, the specification does not disclose any specific and substantial interpretation for the result, and none is known in the art. Given this consideration, the individually claimed polynucleotide has no "well-established" use. The artisan is required to perform further experimentation on the claimed material itself in order to determine to what "use" any expression information regarding this nucleic acid could be put.

With regard to diagnosis of disease, there is no requirement that each and every class of DNA sequences or the proteins they encode have an established correlation with a particular disease. However, in order for a polynucleotide or protein to be useful, as asserted, for diagnosis of a disease, there must be a well-established or disclosed correlation or relationship between the claimed polynucleotide and a disease or disorder. The presence of a polynucleotide in tissue that is derived from cancer cells is not sufficient for establishing a utility in diagnosis of disease in the absence of some information regarding a correlative or causal relationship between the expression of the claimed cDNA or protein and the disease. If a molecule is to be used as a surrogate for a disease state, some disease state must be identified in some way with the molecule. There must be some expression

pattern that would allow the claimed polynucleotide to be used in a diagnostic manner. Many proteins are expressed in normal tissues and diseased tissues. Therefore, one needs to know, e.g., that the claimed polynucleotide is either present only in cancer tissue to the exclusion of normal tissue or is expressed in higher levels in diseased tissue compared to normal tissue (i.e. over expression). Evidence of a differential expression might serve as a basis for use of the claimed polynucleotide as a diagnostic for a disease. However, in the absence of any disclosed relationship between the claimed polynucleotide or the protein that is encoded thereby and any disease or disorder and the lack of any correlation between the claimed polynucleotide or the encoded protein with any known disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner*, 148 USPQ at 696. The disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. §101.

The polypeptide encoded by the polynucleotide of SEQ ID NO:18 belongs is a family in which the members have divergent functions based on which tissues the protein is expressed or administered to. Assignment to this family does not support an inference of utility because the members are not known to share a common utility. There are some protein families for which assignment of a new protein in that family would convey a specific, substantial and credible utility to that protein. For example, some families of enzymes such as proteases, ligases, telomerases, etc. share activities due to the particular specific biochemical characteristics of the members of the protein family such as non-

specific substrate requirements, that are reasonably imputed to isolated compositions of any member of the family.

The diversity of the Calcium channel proteins has already been described. Without some common biological activity for the family members, a new member would not have a specific, substantial, or credible utility when relying only on the fact that it has structural similarity to the other family members. The members of the family have different biological activities which may be related to tissue distribution but there is no evidence that the claimed compounds share any one of diverse number of activities. That is, no activity is known to be common to all members. To argue that all the members can be used for toxicology testing and diagnosis, is to argue a general, nonspecific utility that would apply to virtually every member of the family, contrary to the evidence. Further, any compound could be considered as a regulator or modulator of tissue in that any compound, if administered in the proper amount, will stimulate or inhibit tissue. For example, salt, ethanol, and water are all compounds which will kill cells if administered in a great enough amount, and which would stimulate cells from which these compounds had been withheld, therefore, they could be considered regulators or modulators of tissue. However, use of these compounds for the modulation of tissue would not be considered a specific and substantial utility unless there was some disclosure of, for example, a specific and particular combination of compound/composition and application of such in some particular environment of use.

Without knowing a biological significance of the claimed polypeptides or the polynucleotides or the polypeptide encoded thereby, one of ordinary skill in the art would not know how to use the

claimed invention in its currently available form in a credible "real world" manner based on the diversity of biological activities possessed by the Calcium channel proteins. Contrast *Brenner*, 148 USPQ at 694 (despite similarity with adjacent homologue, there was insufficient likelihood that the steroid would have similar tumor-inhibiting characteristics), with *In re Folkers*, 145 USPQ 390, 393 (CCPA 1965) (some uses can be immediately inferred from a recital of certain properties) or *In re Brana*, 34 USPQ 1436, 1441 (Fed. Cir. 1995) (evidence of success in structurally similar compounds is relevant in determining whether one skilled in the art would believe an asserted utility; here, an implicit assertion of a tumor target was sufficiently specific to satisfy the threshold utility requirement).

The utility must be specific, substantial and credible. Applicants' assertion that the claimed invention has utility in drug screening, testing, drug development and disease diagnosis, do not meet the standards for a specific, substantial, and credible or well-established utility for reasons set forth above.

The specification does not disclose the significance of any test results, nor is there any evidence that the significance was known as of the filing date. If the expression of the claimed polynucleotide increases, is this a positive or negative outcome? Would this be a toxic response or not? The disclosure is insufficient to evaluate the results of the test in any meaningful manner.

Further, Applicant argues that a utility may be specified even if it applies to a broad class of inventions. The proposition is not sufficient to establish utility for each member of the class. Specific utility must be shown or be evident for each member of the class. None of the utilities identified by

Applicant, have been demonstrated to be specific to SEQ ID NO:18 or 19. One of ordinary skill in the art must understand how to achieve an immediate and practical benefit from the claimed species based on the knowledge of the class. However, no practical benefit has been shown for the use of SEQ ID NO:18 or 19.

Applicant argues that practical utility of an invention may be derived from belonging to a broad class of inventions. The requirement in any particular case, however, is that practical utility can be inferred if each and every member of the broad class possesses a common utility.

Applicant has failed with respect to SEQ ID NO:18 and 19, have not described the family or the compounds in enough detail to show, by a preponderance of the evidence, that SEQ ID NO:18 or 19 has any substantial use. The record shows that the Calcium channel protein family is diverse, and has such a broad definition, that a "common utility" cannot be defined. Moreover, the evidence of record is inadequate to determine the disease(s), drug(s) or toxicological screen(s) for which the compounds would be useful. In *Brenner,* the Court approved a rejection for failure to disclose any utility for a compound where the compound was undergoing screening for possible tumor-inhibiting effects and an adjacent homologue of the compound had proven effective. *Brenner*, 148 USPQ at 690. Here, there is no evidence that the claimed isolated compounds have any utility.

For all the above reasons, the disclosure is insufficient to teach one of skill in the art how to use the invention. A review of *In re Wands,* 8 USPQ2d 1400 (CAFC 1988) clearly points out the factors to be considered in determining whether a disclosure would require undue experimentation and include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance

presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. All of these factors are considerations when determining the whether undue experimentation would be required to use the claimed invention. As is evidence in the discussions *supra*, each of these factors has been carefully considered in the instant grounds of rejection, and it is maintained that undue experimentation would be required by the skilled artisan to use the instant invention.

Applicant asserts that the use of the claimed invention drug discovery, and disease diagnosis are substantial utilities. The question at issue is whether or not the broad general assertion that the claimed nucleic acids might be used for *some* diagnostic application in the absence of a disclosure of *which* diagnostic application would be considered to be an assertion of a specific, substantial, and credible utility. For reasons set forth above the disclosure satisfies none of the three criteria *See In re Kirk*, 153 USPQ 48, 53 (CCPA 1967) (quoting the Board of Patent Appeals, 'We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.')

However, for reasons set forth above, Applicant has not presented sufficient evidence to support specific utility for SEQ ID NO:19 or 19. The present rejection under § 101 follows *Brenner v. Manson*, as set forth above. In that case, the absence of a demonstrated specific utility for the claimed steroid compound was not ameliorated by the existence of a demonstrated general utility for the class. Unlike *Fujikawa v. Wattanasin*, where there were pharmaceutically acceptable in vitro results, here, there is nothing other than relatively low levels of sequence homology to a broad and diverse family of proteins having distinct modes of activity, and no disclosed common mode of action. As Applicant recognizes, a rejection under § 112, first paragraph, may be affirmed on the same basis as a lack of utility rejection under § 101. *See, e.g., In re Swartz*, 56 USPQ2d 1703 (Fed. Cir. 2000); *In re Kirk*, 153 USPQ 48 (CCPA 1967).

Therefore, for reasons set forth above, Applicants arguments and exhibits have been fully and carefully considered, but are not considered sufficient to rebut the prima facie case of lack of utility

Claim Rejections - 35 USC § 101 and 35 USC § 112, 1st paragraph

The following is a quotation of 35 U.S.C. 101:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make

and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 28-33 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. Applicants arguments as they pertain to Amended 28-33 have been fully considered but not found persuasive, see above.

A "specific utility" is a utility that is specific to the subject matter claimed, as opposed to a "general utility" that would be applicable to the broad class of the invention. A "substantial utility" is a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. A "well established utility" is a utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. A "well established utility" must also be specific and substantial as well as credible.

Based on the record, there is not a "well established utility" for the claimed invention. Applicant has asserted utilities for the specifically claimed invention of claims 28-33. For example, the specification at page 6 asserts that, "the present invention provides partial sequences for novel mammalian (human and rat sequences identified) calcium channel subunit", and knowledge of the polypeptides encoded by the claimed invention "permits the localization and recovery of the complete

sequence from human cells, and the development of cell lines which express the novel channel proteins of the invention. These cells may be used for identifying compounds capable of acting as agonists or antagonists to the calcium channels". Further stated on page 9, "since defects in the novel calcium channel subunits may be associated with a human genetic disease including, but not limited to; epilepsy, migraine, ataxia, hypertension, arrhythmia, angina, depression, small lung carcinoma. Lambert-Eaton syndrome, characterization of such associations and ultimately diagnosis of associated diseases can be carried out with probes which bind to the wild-type or defective forms of the novel calcium channels". In the applicants arguments filed 6/13/01 no disclosure is made of how to use the polynucleotide of instant invention.

The utilities asserted by Applicant are not specific or substantial. Neither the specification nor the art of record disclose any disease states treatable by the claimed polynucleotides or polypeptides encoded by them. Similarly, neither the specification nor the art of record disclose any instances where blocking any effects of the claimed polynucleotides or polypeptides encoded by them reduces the effect of a disease state. Thus the corresponding asserted utilities are essentially methods of treating unspecified, undisclosed diseases or conditions, which does not define a "real world" context of use. Treating an unspecified, undisclosed disease or condition would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use especially when the complete sequence of the claimed invention is not known. Since neither the specification nor the art of record disclose any activities or properties that would constitute a "real world" context of use for the claimed polynucleotides or the polypeptides encoded by them, further experimentation is

necessary to attribute a utility to the claimed polynucleotides and encoded polypeptides. See Brenner v. Manson, 383 U.S. 519, 535–36, 148 USPQ 689, 696 (1966) (noting that "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing", and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.").

7. Claims 28-33 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Further hybridization conditions of claims 28 are indefinite, as stated in the claim rejection under 35 U.S.C. 112 , second paragraph. The hybridization conditions recited in the claims do not constitute a meaningful structural limitation and the claim recite no functional language. The instant fact pattern closely resembles that in Ex parte Maizel, 27 USPQ2d 1662 (BPAI 1992). In Ex parte Maizel, the claimed invention was directed to compounds which were defined in terms of function rather than sequence (i.e., "biologically functional equivalents"). The only disclosed compound in both the instant case and in Ex parte Maizel is the, naturally occurring compound, polynucleotide represented by SEQ ID NOs: 18, in instant application. The Board found that there was no reasonable correlation between the scope of exclusive right desired by Appellant and the scope of enablement set forth in the patent application. Even though Appellant in Ex parte Maizel urged that the biologically functional equivalents consisted of proteins having amino acid substitutions wherein

the substituted amino acids had similar hydrophobicity and charge characteristics such that the substitutions were "conservative" and did not modify the basic functional equivalents of the protein, the Board found that the specification did not support such a definition, and that the claims encompassed an unduly broad number of compounds. Such is the instant situation. Clearly, a disclosed partial polynucleotide sequence does not support claims to nucleic acid hybridizing to same, given the lack of guidance regarding what sequences would hybridize specifically to the polynucleotide encoding the polypeptide of SEQ ID NOs: 19, and not other, related sequences. Further may of the DAN isolated by hybridization will be incapable of hybridizing to the nucleic acid of SEQ ID NO:18 and encode non-functional protein. Applicant has not disclosed how to use the unrelated polynucleotides or those encoding non-functional polypeptide. Further the claims drawn to cells comprising claimed isolated DNA molecules and method for producing protein from said cells are not enabled for these reasons given above.

Pertaining to Applicants arguments that claims are fully supported by written description in the specification, Applicants arguments have been fully considered but not found persuasive. Applicant states, page 14 of the Amendment, "The Office complains that SEQ ID NO:18 is an "incomplete cDNA." It is an incomplete open reading frame, but this does not mean that it does not permit construction of an expression system for production of a functional protein". Further Applicant further argues, "The essential features of the invention are completely defined since the coding sequence for the functional protein is set forth in sufficient detail to permit the skilled artisan to make a functional protein". In response to Applicants arguments, the Office is not complaining that SEQ

ID NO:18 is an "incomplete cDNA", but merely stating observation made in view of the specification and Applicants, arguments. The specification discloses the polypeptide is incomplete and lacking functionality. Applicants Response filed 6/11/01 verifies the "amino acid sequence encoded by SEQ ID NO:18 is **not complete**", and **lacks a portion of the amino acid sequence which is required to obtain functionality** (See paper number 23, page 4, second paragraph). Therefore, by Applicants own admission, the claimed polynucleotide encoding the polypeptide of SEQ ID NO:19, is incomplete. Applicant further admits, page 6, the **polypeptide is missing "approximately 400 amino acids**". Even though the missing sequence may turn out to be homologous or similar to the C-terminus of other cannel proteins, further experimentation is required to complete the missing sequence. The claims are drawn to species of polynucleotide encoding functional protein. There is no disclose of the critical feature of the invention that is required for activity. In conclusion Applicants invention is a polynucleotide encoding a partial sequence of a polypeptide who's functionality has yet to be determined but the claims are drawn to species of DNA encoding "functional T-type, low voltage activated calcium channel $\alpha 1$ subunit", which clearly does not meet the written description requirement of the invention in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing.

8 Claims 28-33 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant specification does not contain a written description of the invention in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing.

Examiner has assumed claims 28-33 are directed to DNA comprising fragments encoding functional polypeptide of SEQ ID NOs: 19, polynucleotides that hybridize to said fragments, cells contain said fragments and methods of producing calcium ion channel protein, because the claims as written refer to SEQ ID NOs 18 as polypeptides, whereas they are polynucleotides.

The claims are drawn to isolated DNA molecules encoding **functional** T-type, low voltage activated calcium channel $\alpha 1$ subunit

a) comprising SEQ ID NOs: 19

b) encoded by nucleic acid that hybridizes to DNA molecule encoding SEQ ID NOs: 19 or by the nucleic acid of SEQ ID NO:18.

The claims are further drawn to cells containing a) or b) and method of producing calcium channel protein using c)

The specification, on page 9, lines 14-16, discloses instant application contains partial polynucleotide sequences of a calcium channel subunit and the applicant indicates, "These subunits are believed to represent two new types of α_1 subunits of human voltage-dependent calcium channels

which have been designated as type α_{1I} and type α_{1H}", and further states, "The novel α_1 subunits of the invention were identified by screening the *C. Elegans* genomic DNA sequence data base for sequence homologous to previously identified mammalian calcium channel α_1 subunits. The specification discloses isolated cDNA sequence, SEQ ID NO: 18 encoding the polypeptide of SEQ ID NO:19. Applicant had admitted that each of the SEQ ID NOs: 18 and 19, elected for examination are incomplete, without known functionality . Because the cDNAs that correspond to the SEQ ID NOS mentioned in the claims are not full-length, a sequence prepared from undefined parts of a cDNA clone will not comprise the entire coding region of any particular gene, nor is it clear the partial sequence is even in frame to encode a polypeptide. The specification nor prior art discloses that the DNA claimed encodes a functional protein, nor what that function is. The claims, as written, however, encompass polynucleotides which vary substantially in length and also in nucleotide composition. The broadly claimed genus encompasses functional calcium ion channel polypeptides genes whose encoded protein, as well as genes incorporating only portions of the disclosed sequence as well as chimeric constructs and variants.

The instant disclosure of a single species of nucleic acid does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera including full-length genes. A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly &*

Co., 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of polynucleotides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. The specification proposes to discover other members of the genus by using hybridization techniques. There is no description, however, of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides encompassed and no identifying characteristic or property of the instant polynucleotides is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed.

The specification further fails to identify and describe the 5' and 3' regulatory regions and untranslated regions essential to the function of the claimed invention, which are required since the claimed invention currently encompasses the gene. The art indicates that the structures of genes with naturally occurring regulatory elements and untranslated regions is empirically determined. Therefore, the structure of these elements is not conventional in the art and skilled in the art would therefore not recognize from the disclosure that applicant was in possession of the genus of nucleic acid, including genes, comprising SEQ ID NO: 18 or fragments thereof. Further vectors containing

genomic DNA nor cells containing said vectors are disclosed. Further methods of using said genomic DNA are rejected for the reasons given above.

Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of specific nucleotide sequences and the ability to screen, is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed. Although the nucleotide of SEQ ID NO:18 may encode a α_1 subunit of calcium channel the disclosure no prior art disclose any polynucleotides that may bind the polynucleotide of SEQ ID Nos:18 and encode functional α_1 subunit of calcium channel.

An adequate written description of a DNA, such as the cDNA of instant application, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel* , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606. (page 1404)

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal Basi whose telephone number is (703) 308-9435. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 308-0294.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nirmal S. Basi
Art Unit 1646
October 21, 2001

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600